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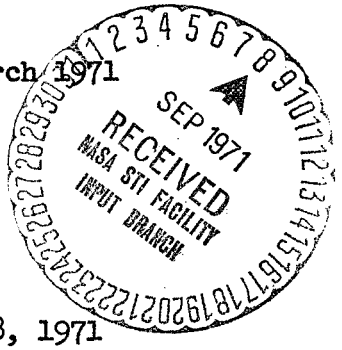

NASA CONTRACT NO. NSR 05-018-087
(USC No. 53-5137-1449)

PROGRESS REPORT

Period Covered: December 1, 1970 through February 28, 1971

SUMMARY

During this reporting period major efforts were directed toward flow probe development, redesign of pressure and flow electronics, and evaluation of flow probes and the redesigned electronics through use of implants.

FLOW PROBE DEVELOPMENT

The commercial flow probes used in previous testing have proven unsatisfactory due to structural inadequacies. To overcome this problem at minimum expense techniques of fabricating structural sound flow probes have been developed by the staff. Several probes have been built and tested in acute animal preparations. These probes are made from stock cast acrylic rods which are fitted with ultrasonic crystals. The crystals are placed diagonally across a smooth lumen. The result is a rugged probe with well controlled dimensions. An additional advantage of the smooth lumen probe is that flow data can be obtained shortly after implant, as acoustical contact with the vessel wall and the flow stream is immediately developed.

The old probe required several days to develop good acoustical contact due to the time required for tissue to fill the cavity where the crystals were mounted.

ELECTRONIC DEVELOPMENT

In order to reduce the size of the implant package necessary for measurement of flow and pressure, a redesign of the basic electronics was undertaken. This has resulted in a reduction in current and voltage requirements and an attendant decrease in size. The current two-channel system has a volume of approximately 3.5 cubic inches.

PACKAGE FABRICATION

A totally implantable two-channel telemetry system consisting of blood flow and blood pressure has been fabricated. This unit employs the newly fabricated probe and electronics. It has a predicted operating life of 100 hours and is currently programmed to remain on for 8 minutes when turned on by an RF signal. Under these conditions 750 activations are available. At two activations per day, an operating duration of nearly a year can be predicted. The transmitting duration can be controlled as desired by a resistor selection prior to implant. As an example, the transmitting duration could be adjusted to 1 minute and data obtained once each hour for approximately 250 days.

EXPERIMENTS

Two major experiments were conducted during this period. The new package was implanted in a dog in February for an acute evaluation. A commercial flow probe was employed and unfortunately failed; however pressure was obtained for a period of two weeks. The package was reimplanted with a new flow probe attached on March 8, 1971. The intent is to obtain data from this implant at least once each day while useful data is being recorded.

DOCUMENTATION

A copy of a paper describing an earlier version of a two-channel telemetry system is submitted with this report. A complete description of a more recently completed two-channel system is being prepared. This description will be forwarded when completed.

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JPM/jk

CARDIOVASCULAR TELEMETRY IMPLANTS

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ABSTRACT

Several measurement problems unique to biological experiments have their solution in telemetry. The development of telemetry techniques to solve these measurement problems has resulted in totally implanted systems. An explanation of these measurement problems, a description of the equipment developed to solve the problems, and the technique for applying the equipment is presented in this paper.

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ACKNOWLEDGMENTS

John Henriksen's assistance in circuit and package design is gratefully acknowledged. This work was supported by NASA Contract NSR-05-018-087.

INTRODUCTION

Measurement accuracy is as necessary in obtaining meaningful research results in the life sciences as it is in the physical sciences. Caution must be exercised in conducting any measurement in order to insure that the application of the measuring device does not excessively disturb the quantity being measured. An additional concern arises in conducting measurements on animals as both the very act of bringing the animal into a measurement situation and the often traumatic application of the measuring device to the subject can produce an emotional reaction which influences the value of the parameters being studied. To minimize this emotional reaction, drugs are often administered with the result that the parameter under investigation may be altered. In many cases neither option: the application of the measuring devices without the benefit of anesthesia, nor the administration of drugs to control the subject's reaction to measurement application yields a valid experimental situation. The escape from this experimental dilemma has led to the use of biotelemetry. The subject can then be instrumented under anesthesia and after sufficient recovery be monitored under more natural conditions. The application of telemetry as a tool for improving measurement techniques is expanding and is currently credited as being one means of acquiring data from near-normal, unrestrained unanesthetized animal subjects(1).

In an efficient measuring system parameter selection is often made on the basis of maximum information yield relative to other constraints, such as minimum power expenditure, acceptable accuracy,

and minimization of size. In cardiovascular research parameter selection is made on the basis that knowledge of blood pressure and blood flow is required for appreciating the hemodynamics of the circulation to the body as a whole or to any organ in particular. Measurement of these two parameters yields considerable direct information and other parameters can be calculated. In addition to heart rate, dynamic pressure measurements yield information about the heart contractility and the elasticity of the vessels. Dynamic blood flow measurements conducted on the ascending aorta yield cardiac output in liters per minute from which an appreciation for the availability of nutrients to the tissue can be realized. From the ratio of arterial pressure to arterial flow an estimate of flow resistance can be obtained; and since this resistance is modulated in part by nervous system inputs, a prediction of the involvement of the central nervous system in the cardiovascular regulation can be made.

Measurement of these two parameters, flow and pressure, in unrestrained ambulatory animals is improved by the use of totally implanted telemetry devices. It is the problem of the designer to achieve a telemetry device meeting conditions relating to size, operating life, accuracy, and reliability which satisfies the experimental requirements. The necessity for implant imposes stringent conditions. An equipment package size compatible with subject size is a major controlling requirement. With a fixed package size operating life can only be increased by limiting power consumption; thus the use of low power electronics is necessary and some form of transmitter control is indicated. Reliable maintenance-free operation is also very important; as once the unit is

implanted, repair can be conducted only by removing the implanted electronics. Electronic and sensor stability is also of major importance as frequent calibration cannot be readily performed.

INSTRUMENTATION DESIGN

In this application a frequency modulation mode of telemetry is employed; therefore a telemetry system will have common to all channels a carrier oscillator, batteries, and associated power controllers necessary for control of transmission. Each individual channel will then require a signal conditioner and a frequency modulated subcarrier oscillator. The design of the carrier and subcarrier oscillator is an important aspect of the total system, but will not be presented here as these units have been previously described elsewhere (2). The design of pressure and flow signal conditioners and associated sensors is considered in this paper.

In this development one of the more important factors has been the realization of low current operation in conjunction with small size and good thermal and time stability. Since a frequency modulated telemetry system is employed the outcome of the electronic development has been a frequency modulated subcarrier oscillator proportional to either pressure or flow.

Blood Pressure Signal Conditioner

Detection of blood pressure was accomplished by the use of chronically implanted miniature pressure sensors* (3). The sensor body is unalloyed titanium 6.5 mm in diameter and 1 mm thick. This material

* Manufactured by Konigsberg Instruments, Pasadena, California.

is highly corrosion-resistant allowing long term direct contact with body fluids. Four semiconductor strain gauges, connected in a conventional four-arm bridge, are bonded to the inner surface of the small pressure-sensing diaphragm. Positive pressure on the face of the transducer causes resistance changes which are transformed to a voltage change. The sensor is quite sensitive, producing approximately 30 mv/300 mm Hg when used as suggested by the manufacturer. Its frequency response is well in excess of that required to obtain dynamic blood pressure measurements and its temperature characteristics can be determined and properly dealt with.

Figure 1 illustrates a circuit schematic which transforms blood pressure variations to voltage variation and sequentially produces frequency modulation of a subcarrier oscillator proportional to pressure. It consists of a differential input voltage-controlled oscillator with active elements Q_5 and Q_6; a pulse generator consisting of active components Q_1, SCS_1, and Q_4; and a pulse-amplifying circuit consisting of Q_2 and Q_3. The output of the voltage-controlled oscillator turns SCS_1 on, which turns Q_4 on, placing the supply voltage across the pressure sensor. Transistor Q_1 turns on after a delay established by the RC time constant and turns SCS_1 off. The effect is then an application of a narrow voltage pulse to the pressure sensor on each positive excursion of the voltage-controlled oscillator output. The difference between the pulse levels at the output of the pressure sensor is amplified by Q_2 and Q_3 and filtered by the RC networks connected to the collectors. The resulting DC voltage, which is proportional to the pressure applied to the transducer, is then employed to modulate the

voltage-controlled oscillator. Major advantages of this mode of operation are high sensitivity, low current operation, and the realization of overmodulation protection by the use of a subcarrier with frequency limits (2).

Frequency limits beyond which the oscillator cannot be modulated are realized by operating two parallel-T oscillators with different frequency of oscillations in parallel with a common collector load. If either transistor is completely cut off, the frequency of oscillation is determined by the circuit connected to the base of the other. When both transistors are conducting equally the frequency is near the average of the two specific frequencies.

Blood Flow Signal Conditioner Concept

Flow detection by an ultrasonic technique was selected because of several clearly identifiable advantages. As contrasted with the electromagnetic techniques, the ultrasonic flow sensing probes are lighter, power requirements are less, and the signal level is higher.

The prototype system developed in this laboratory is illustrated in Figure 2a (4). Two crystals placed across a flow section are excited in phase opposition by a continuous 5 mHz signal. The ultrasonic energy from X_1 impinging on X_2 casuses a voltage to sum with the basic excitation voltage on X_2. The same is true of X_2 to X_1. These signals are either delayed or advance in time and therefore modulated in phase proportional to flow. Ideally voltages e_1 and e_2 are:

$$e_1 = V\cos 2\pi ft - K_1 V\cos 2\pi ft + \delta + \theta$$

$$e_2 = V\cos 2\pi ft + K_1 V\cos 2\pi ft + \delta - \theta$$

where the cross coupled components are:

$-K_1 V\cos\ 2\pi ft + \gamma + \theta$ (energy received at X_1, generated by X_2)

$K_1 V\cos\ 2\pi ft + \gamma - \theta$ (energy received at X_2, generated by X_1)

and K_1 is an attenuation factor related to the distance and material between crystals and to the Q of the crystals; f is the frequency of excitation; θ is a phase shift caused by the flow; and γ a phase shift related to probe geometry. The output voltage is then:

$$e_s = \left[2K_1 V\sin\ \theta\right] \sin\ 2\pi ft + \gamma$$

The magnitude of the signal voltage is thus a function of sine θ. The value of θ and γ can be derived by considering the probe geometry and the flow velocity. In particular, the approximate time required for energy to radiate from X_1 to X_2 is:

$$T_{1-2} = \int_o^d \frac{dx}{C + v\cos\alpha}$$

Where C is the velocity of the acoustical energy in the body fluids and tissue, α is the angle between the flow velocity and the energy direction, v is the velocity of blood flow, and d the distance between crystal faces. Division of

$$\frac{1}{C + v\cos\alpha}$$

results in

$$\frac{1}{C}\left[1 - \frac{v\cos\alpha}{C} + \left(\frac{v\cos\alpha}{C}\right)^2 - \left(\frac{v\cos\alpha}{C}\right)^3 \cdots\right]$$

By the valid assumption that

$$\frac{v\cos\alpha}{C} \ll 1$$

the higher power terms can be neglected to give

$$T_{1-2} = \frac{d}{C} - \frac{v\,d\cos\alpha}{C^2}$$

The total phase shift between the crystal signal and the primary drive signal is the delay time divided by the period of the excitation voltage:

$$\gamma - \theta = \frac{T_{1-2}}{T} = \frac{2\pi fd}{C} - \frac{2\pi fvd \cos\alpha}{C^2}$$

where f is the drive signal frequency.

Thus

$$\gamma = \frac{2\pi fd}{C}$$

$$\theta = \frac{2\pi fvd \cos\alpha}{C^2} .$$

The output voltage then becomes:

$$e_s = 2 \frac{K_1 V \sin 2\pi fvd \cos\alpha}{C^2} \sin \left(2\pi ft + \frac{2\pi fd}{C} \right)$$

The factor $2\pi fd/C$, a phase related to probe dimensions and excitation frequency, contributes no information regarding flow velocity.

The function $2\pi fvd \cos\alpha/C^2$ contains the useful flow information and produces amplitude modulation of the signal proportional to the sine of the function. For a low value of velocity the phase shift produced is small, allowing sine θ to be replaced with θ The signal amplitude then becomes:

$$E = \frac{4\pi f K_1 V vd \cos\alpha}{C^2} = K_o v$$

For 1 cm lumen probes and low level probe excitation voltages the value of K_1V has been found to be nominally 0.5 volt. The value of K_o thus becomes approximately 0.3×10^{-3} and the signal level is then:

$$E = 3\ v \times 10^{-4} \text{ volts/cm/sec}$$

For flow measurement on a 1 cm diameter vessel with a flow velocity of 100 cm/sec, a 30 mv signal can be realized. This can be contrasted with an electromagnetic level of 0.5 mv for the same position and a pickup signal on the order of several tens of microvolts for the back scatter ultrasonic technique (5). The selection of the 180 degree quiescent phase difference between the crystal voltages results in excellent sensitivity. In practice the flow velocity is quite low producing a maximum phase shift of less than 0.1 radian; the substitution of θ for sine θ contributes negligible error and a linear relationship between flow velocity and output signal exists.

Blood Flow Signal Conditioner Circuit

To achieve power consumption compatible with long term implant considerably lower current operation is necessary. The block diagram in Figure 2b illustrates the operation of such a low power system. As in the prototype circuit, piezoelectric crystals resonant at 5 mHz are rigidly positioned diagonally across a flow section. In this case the crystals are electrically pulsed simultaneously in phase opposition for approximately 1 microsecond; crystal excitation therefore ceases prior to arrival of cross coupled energy, and measurement is conducted only on the response of the crystals to cross coupled energy. If the flow is zero, the time required for the acoustical energy to arrive at X_2 from

X_1, and X_1 from X_2 is equal and therefore remains in phase opposition resulting in cancellation of the pickup signals. If the flow velocity is not zero and directed to the right, the energy from X_1 to X_2 arrives in advance of that from X_2 to X_1 resulting in a phase shift and noncancellation of the crystal voltages. Specifically, if the crystal excitations are bursts of sinusoidal voltage defined during the bursts by:

$$e_1 = V\cos 2\pi ft$$

$$e_2 = -V\cos 2\pi ft$$

then the crystal pickup voltages are signal bursts delayed in time by the transit time between crystals and modulated in phase relative to each other by the flow velocity. Specifically the pickup voltages are:

$$e_1 = -K_1 V\cos 2\pi ft + \delta + \theta$$

$$e_2 = K_1 V\cos 2\pi ft + \delta - \theta$$

where K_1, δ, and θ are defined as in the previous case. If the two signals are added as in the illustration and sine θ replaced with θ, the signal amplitude at the output of the summing amplifier becomes:

$$E = \frac{A_o\, 2\pi f\, K_1 V\, vd\, \cos\alpha}{C^2}$$

For a 1 cm lumen probe the signal is:

$$E = 3A_o\, v \times 10^{-4} \text{ volts/cm/sec}$$

Except for the summing amplifier gain, this approach yields the same basic sensitivity as was obtained by the previously described method. Detection of the signal voltage is slightly altered due to the pulsed nature of the crystal excitation.

The circuit required to perform the operation illustrated in Figure 2b is shown in Figure 3. The output of a subcarrier oscillator is connected to the cathode gate of SCS_1. When the gate voltage rises above 0.7 volt, SCS_1 turns on and forward-biases the 5 mc oscillator transistor Q_2 and the 5 mc power amplifier transistor Q_1. Coincidental with the SCS_1 turn-on capacitor C_7 starts to charge through R_{12}. When Q_3 is sufficiently forward-biased, SCS_1 turns off leaving a charge on C_9 which in turn charges C_{11} through R_{15} turning on SCS_2. This turns on the amplifier transistors Q_6, Q_7, Q_8, and Q_9 just prior to the arrival of the incident acoustical energy at each crystal. The on time of the amplifiers is controlled by the time constant determined by R_{20} and C_{14}. The RC network connected to the emitter of Q_9 rectifies and filters the amplified RF signal, producing a DC signal proportional to flow velocity. The output is then connected to the subcarrier oscillator to produce frequency modulation proportional to flow velocity.

For an ideal case where the crystals are well matched and the summing resistances are equal, the response curve is an absolute value function and reverse as well as forward flow appear as a positive voltage. A small capacitor placed in parallel with R_1 leads to an improved measurement as the pickup signal on X_2 then leads the pickup signal on X_1 and thus for zero flow there appears to be a flow from X_1 toward X_2. Therefore at zero flow there is a positive voltage getting more positive for forward flow and less positive for reverse flow. Since the maximum negative flow is quite small, only a slight adjustment is required to acquire the ability to measure reverse flow.

Application

In order to realize reliable implantable devices which will operate for several months it becomes necessary to limit the transmission time to a small percentage of the intended implant life. A radio frequency actuated switch which enables the telemetry system to be commanded by the investigator is one solution. Transmitted energy is received and detected by an inductance capacitance tuned circuit in the base circuit of a high gain amplifier. The amplifier turns on a silicone control switch one which has approximately a 4-minute on time. This mode of operation allows command of transmission and insures against battery decay due to accidental turn on by extraneous sources.

Figure 4 illustrates a prototype package with pressure sensor and flow probe attached. Each amplifier, voltage regulator, power controller, and oscillator was assembled and potted, then interconnected within the package. The package was fabricated from cast acrylic and the cover was attached by screws and sealed with an O-ring. The pressure sensor and flow probe were attached to the package by removable miniature connectors. Used with a 160 ma hour battery the unit pictured will operate continually for approximately 50 hours. The controller was set to 4 minutes resulting in a potential of 750 actuations. At an average of two recording events per day an operating life of slightly over one year is available.

Figure 5 illustrates a sample recording obtained from a total implant on a small dog. The flow probe was placed about the abdominal aorta and pressure sensor within the same vessel. After proper recovery the connectors were exposed and connected to the transmitter instrument

package. The instrument package was placed intramuscularly in the abdomen. Calibration of the flow was accomplished prior to implant by placing the probe in a fixture and forcing known quantities of fluid through in varying times. The nominal sensitivity was 0.1 volt output per ml/sec. Pressure calibration was conducted prior to implant by standard manometric techniques. Pressure recalibration can be conducted after implant by comparing the transmitted pressure to pressure obtained by cannulation.

DISCUSSION

The inherent disadvantages of hardwire techniques used to measure blood pressures and blood flow in unrestrained animals have been briefly considered; and it is clear that they do little to reduce the complexity of separating psychological factors from the physiological parameters under investigation. This is not to deny that emotional influences may be involved in many physiological reactions, but if the response is to be quantified, the emotional variable must be controlled. The advantages of using remote recording in studies which demand complete relaxation and freedom of the animal are evident. Telemetry also permits the necessary latitude for investigating the cardiovascular responses under broad environmental conditions; and certainly if the effects of social interaction and behavior on cardiovascular dynamics are to be thoroughly investigated, telemetry offers an improved approach.

The implanted miniaturized system used in this study even further eliminates clouding of the data by emotional responses which occur in animals with other procedures and permits a more valid interpretation of

the influence of the manipulated variable on physiological function. The implant method also allows a better definition of normal physiological baseline conditions and eliminates the many problems associated with both hardwire and external telemetry techniques. The equipment described appears to have widespread application in chronic studies. It is apparent therefore that the collection of quantitative and qualitative blood pressure and blood flow data on free-roaming animals is now obtainable with the use of implant telemetry techniques.

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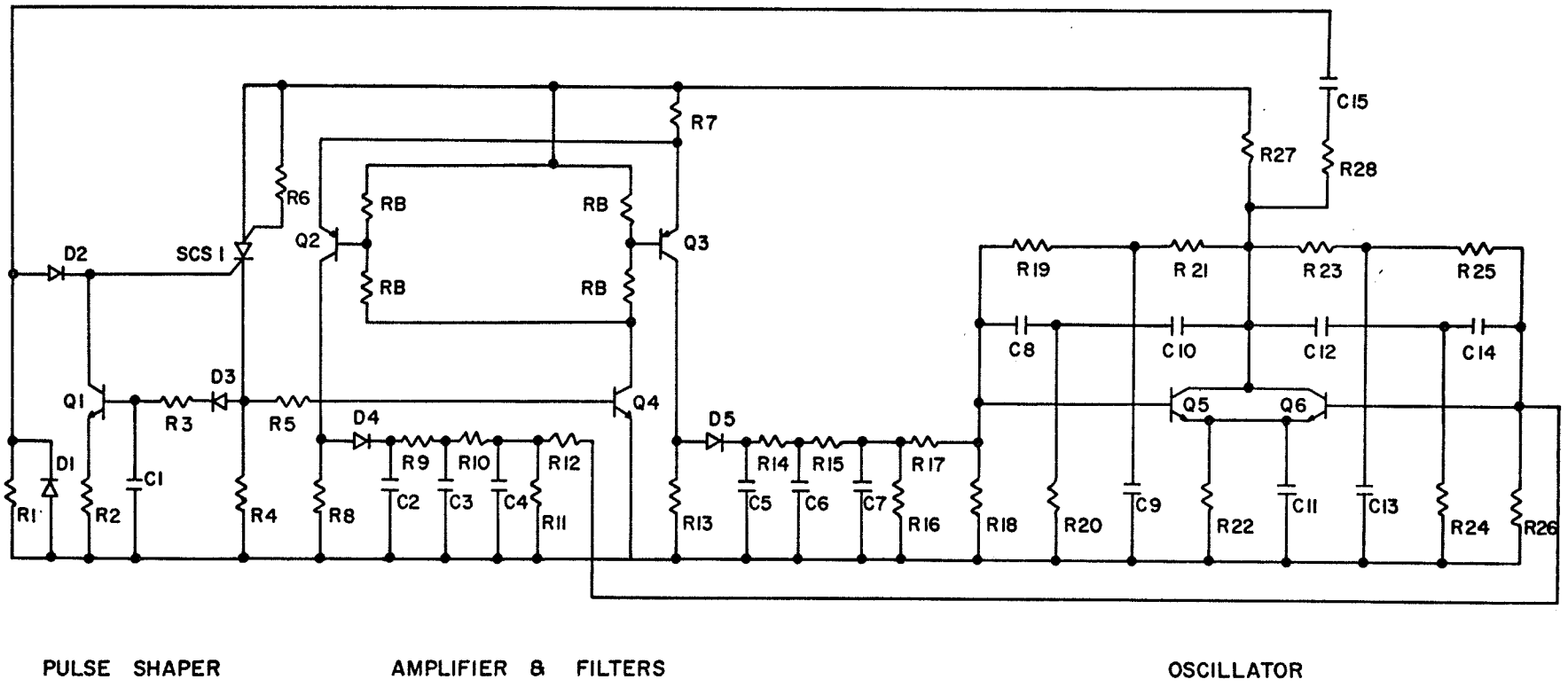


Fig. 1. Blood Pressure Circuit Schematic

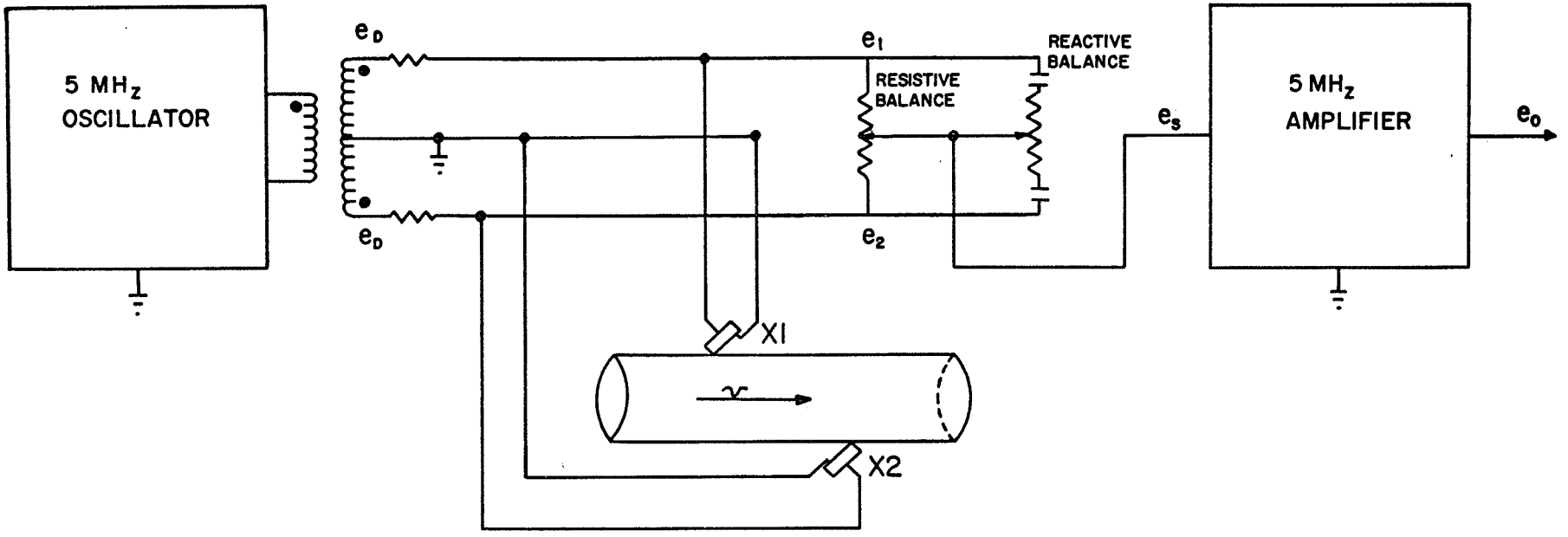
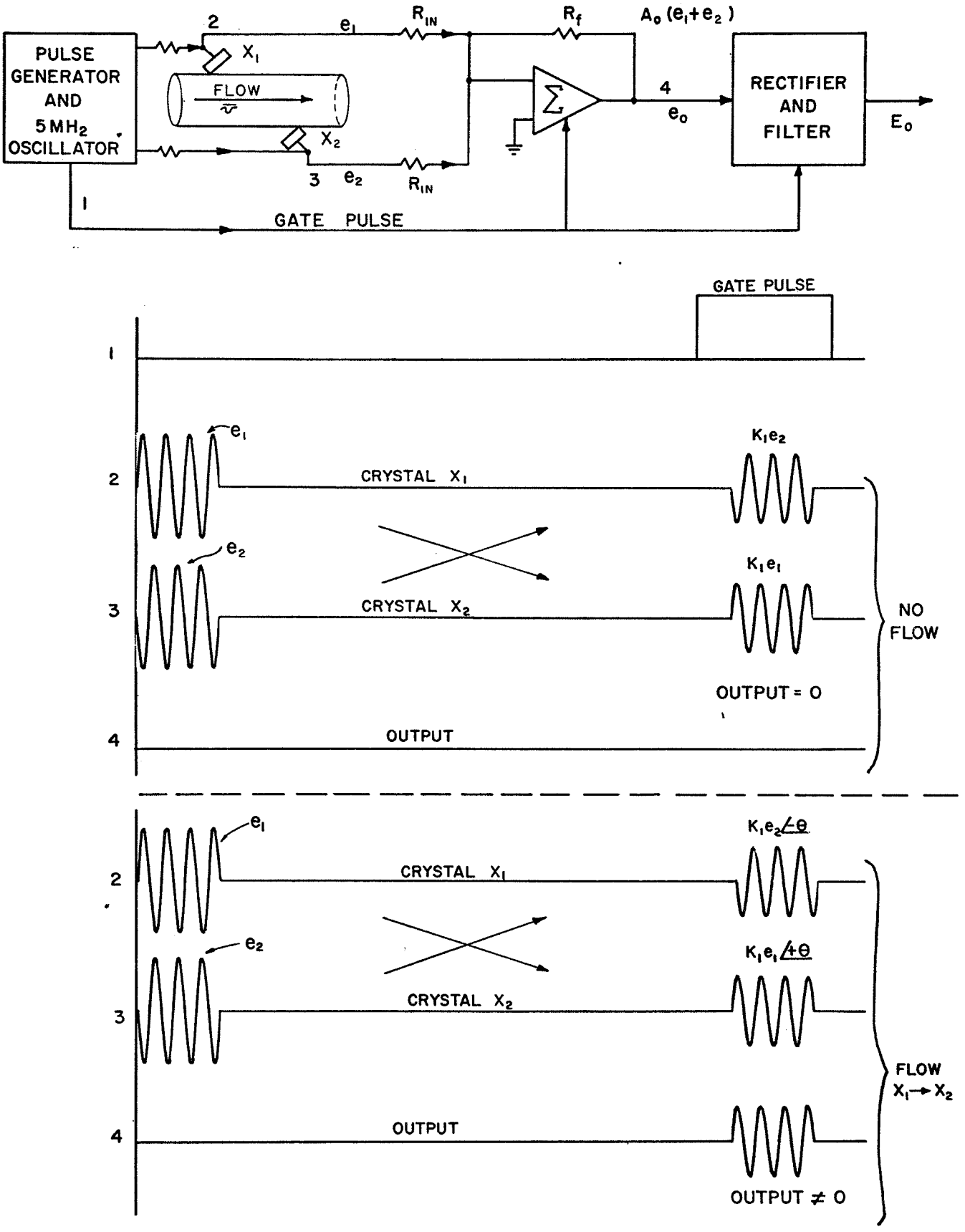


Fig. 2a. Block Diagram of Blood Flow Signal Conditioning Concept



BLOOD FLOW BLOCK DIAGRAM

Fig. 2b. Block Diagram of Low Power Blood Flow Signal Conditioning Concept

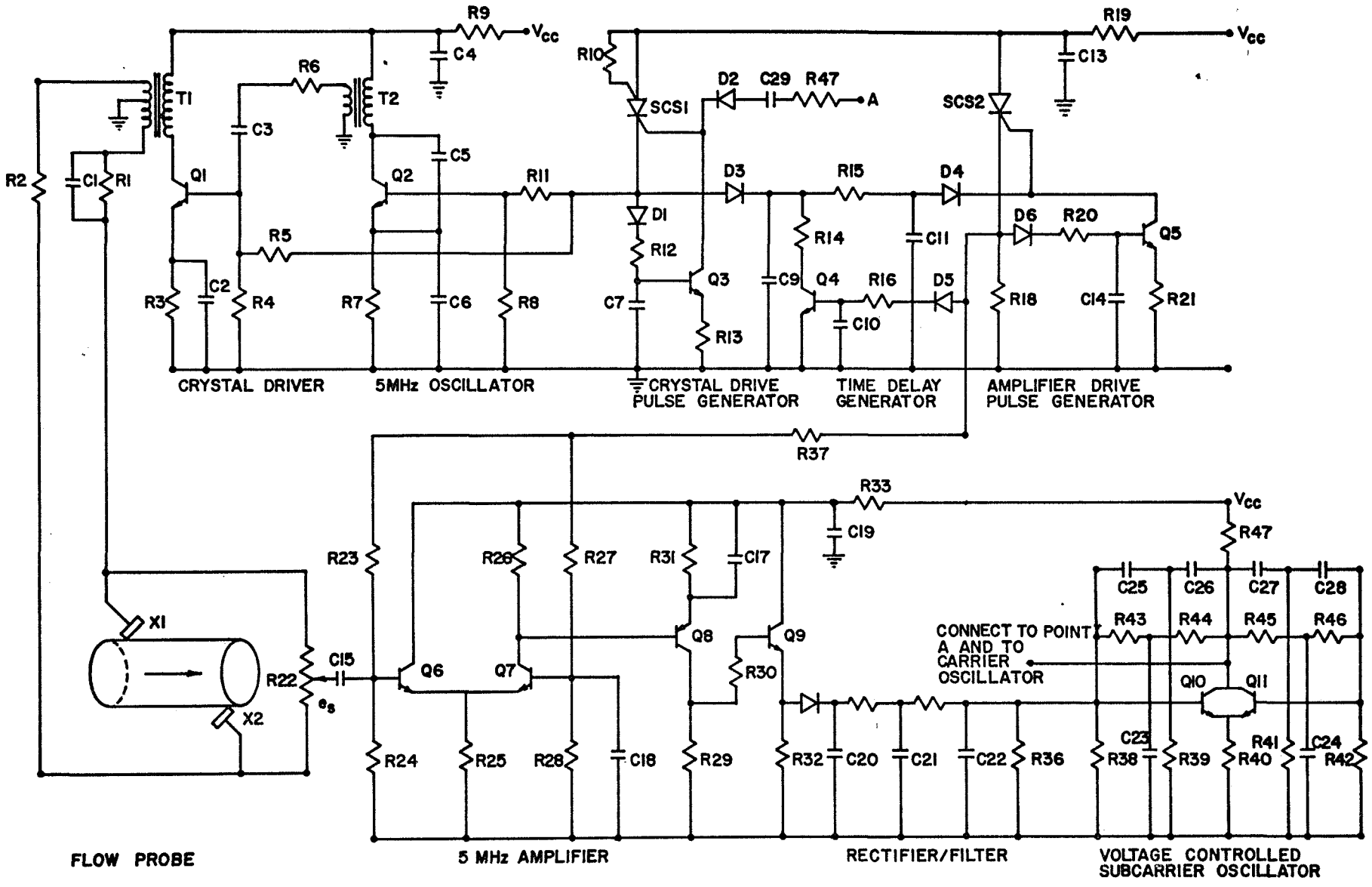


Fig. 3. Low Power Blood Flow Signal Conditioner Circuit Schematic

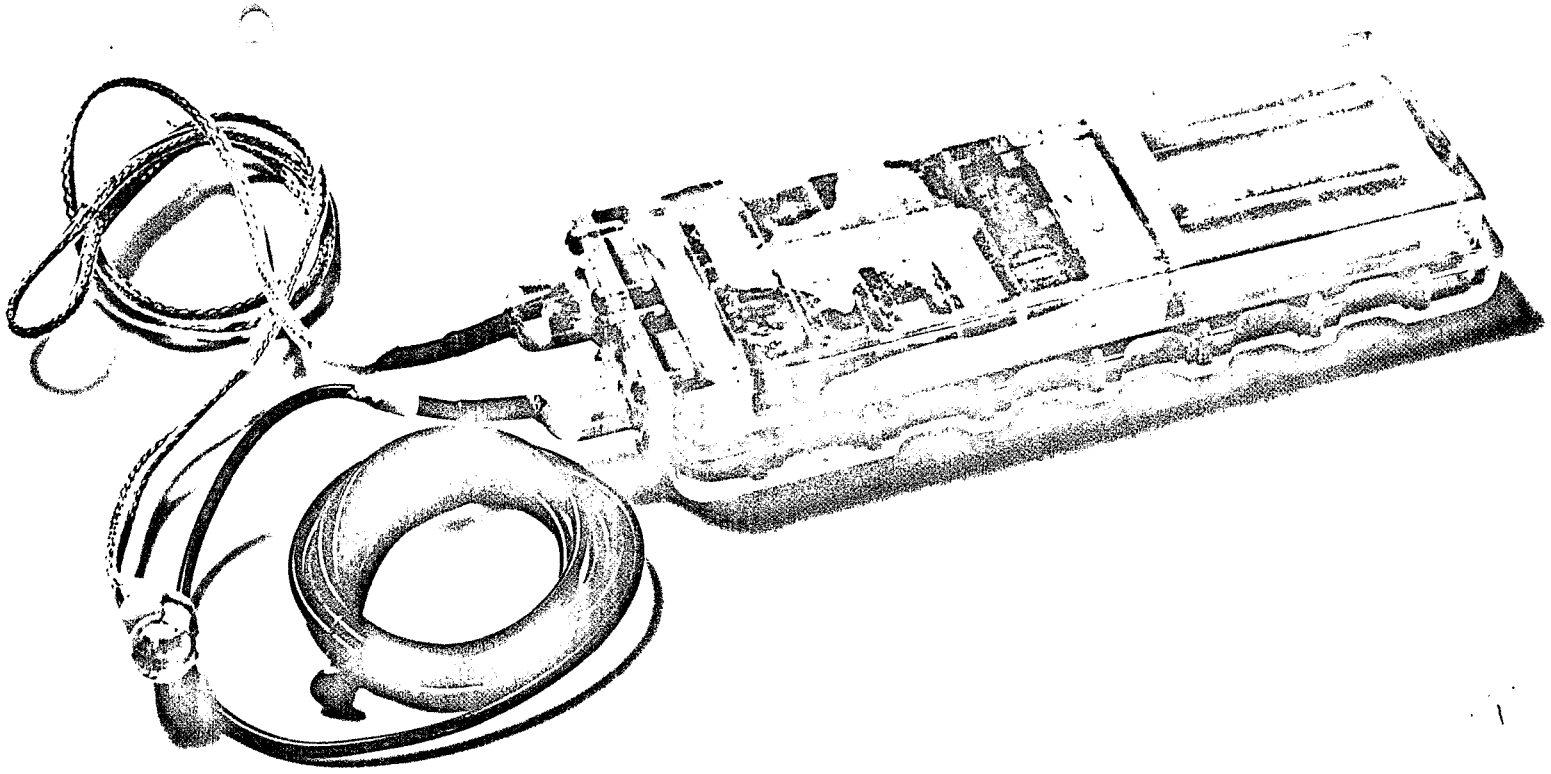


Fig. 4. Assembled Implantable Flow and Pressure Transmitter